The Efficacy of a Lateral Wedge Insole for Painful Medial Knee Osteoarthritis After Prescreening: A Randomized Clinical Trial

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Objective. Lateral wedge shoe insoles decrease medial knee loading, but trials have shown no effect on pain in medial knee osteoarthritis (OA). However, loading effects of insoles are inconsistent, and they can increase patellofemoral loading. We undertook this study to investigate the hypothesis that insoles would reduce pain in preselected patients.

Methods. Among patients with painful medial knee OA, we excluded those with patellofemoral OA and those with a pain rating of <4 of a possible 10. We further excluded participants who, in a gait analysis using lateral wedges, did not show at least a 2% reduction in knee adduction moment (KAM), compared to wearing their shoes and a neutral insole. We then randomized subjects to lateral wedge versus neutral insole for 8-week periods, separated by an 8-week washout. The primary outcome measure was knee pain (0–10 scale) during the past week, and secondary outcome measures included activity pain and pain rated in the Knee Injury and Osteoarthritis Outcome Score questionnaire. We carried out mixed model analyses adjusted for baseline pain.

Results. Of 83 participants, 21 (25.3%) were excluded from analysis because of insufficient reduction in KAM. In the 62 patients included in analysis, the mean ± SD age was 64.2 ± 9.1 years, and 37.1% were women. Lateral wedge insoles produced a greater reduction in knee pain than neutral insoles (mean difference of 0.7 on 0–10 scale [95% confidence interval 0.1, 1.2]) (P = 0.02). Findings for secondary outcome measures were mixed.

Conclusion. In participants prescreened to eliminate those with patellofemoral OA and biomechanical nonresponders, lateral wedge insoles reduced knee pain, but the effect of treatment was small and is likely of clinical significance in only a minority of patients. Targeting patients may identify those who respond to this treatment.

INTRODUCTION

Approximately 12% of people age 60 and over have painful knee osteoarthritis (OA) (1). Rates of knee replacement have been rising in large part because of the failure of medical and rehabilitative treatments. New treatments for knee OA are badly needed.

Lateral wedge insoles placed inside shoes laterally shift loading across the knee during walking. They reduce the load across the medial knee, where most affected individuals have either isolated disease or disease combined with involvement of the patellofemoral (PF) joint. Lateral wedge insoles reduce the external knee adduction moment (KAM), a measure of the load across the medial versus lateral compartments, by 5–6% (2,3). Unfortunately, in trials, lateral wedges have not demonstrated a reduction in knee pain, compared to neutral insoles. In a meta-analysis by Parkes et al (4), 8 randomized controlled trials comparing lateral wedge insoles to neutral insoles produced null results, and the effect size on pain reduction was 0.03 (95% confidence interval [95% CI] −0.18, 0.22). A subsequently published trial also produced negative findings (5).

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In 25% of patients, the wedge does not reduce medial load (6,7). Furthermore, OA in the PF joint may worsen as load is shifted laterally. We therefore hypothesized that if we selected individuals with painful medial compartment knee OA who showed a biomechanical response to wedge insoles and did not have painful PF OA, they would experience a reduction in knee pain with these insoles compared to neutral insoles.

Because the use of a shoe insole is a simple, low-cost intervention, its efficacy in reducing pain could translate into a substantial public health benefit and possibly into widespread use. Further, medial knee OA is highly prevalent not only in Western countries but in developing countries where knee replacement surgery is not widely available. We conducted a crossover trial testing a 5° lateral wedge insole, which is the same insole we and others previously tested (8).

PATIENTS AND METHODS

Recruitment and eligibility. *Recruitment*. This study was a randomized trial (registration no. ISRCTN55059760) that tested lateral wedge insoles and neutral insoles in persons with painful medial knee OA. The protocol was approved by National Research Ethics Service Committee North West (Preston, UK). Subjects were recruited from general practices and by way of advertisements in Manchester, UK from January 2016 through June 2017.

Inclusion criteria. We instituted the following eligibility criteria: ages 40–85 years; severity of overall knee pain (the primary outcome measure) in the past week of ≥4 on a 0–10 grading scale, and Kellgren/Lawrence (K/L) (9) grade of 2–4 in the painful knee (as scored by a musculoskeletal radiologist) on a posteroanterior or anteroposterior radiograph obtained within the last 2 years that showed definite medial (but no definite lateral) narrowing. Patellofemoral OA had to be less severe than medial OA and could not have a K/L grade of ≥3. Additional inclusion criteria included medial joint line tenderness (with tenderness over the patella less severe than medial tenderness) upon examination by an experienced physical therapist (MJC), a stable medication regimen for 3 months, and a willingness to wear insoles in shoes for ≥4 hours daily.

Exclusion criteria. Subjects were excluded for the following reasons: a history of high tibial osteotomy, other realignment surgery, or knee replacement in the painful knee, knee arthroscopy within the last 6 months, or an intraarticular injection of either steroid or viscosupplementation in the affected knee within the past 3 months. People with the following disorders or conditions were also excluded: rheumatoid arthritis or other inflammatory arthritis, diabetic neuropathic pain or fibromyalgia, foot or ankle problems that contraindicated the use of load-modifying interventions in footwear, or severe coexisting medical morbidities. Further exclusions included inability to walk unaided without a crutch, cane or walker, body mass index (BMI) ≥35 kg/m^2, and current use of or need for foot orthoses. We also excluded those who were unable to retain information regarding study procedures or were unable to walk 100 meters without stopping. A secondary outcome measure was change in magnetic resonance imaging (MRI) features, and those with contraindications to MRI were also excluded, as were those with knee surgery planned within the next 6 months.

Evaluation and treatment. For eligible subjects, a gait laboratory appointment was made. At the time of this appointment, subjects were randomized remotely for the order of testing of insoles in their shoes (no insole, neutral insole, or lateral wedge insole). A 10-camera Qualisys ProReflex motion analysis system operating at 100 Hz and 2 Kistler force plates operating at 1,000 Hz were used to measure kinematics and kinetics. Each subject participated in a minimum of 5 successful trials (defined as when a single foot contacted the force plate). The Calibrated Anatomical Systems Technique marker set technique (10) was used (8). Retroreflective markers were mounted securely to participants' shoes, with the foot modeled as a rigid segment. Ankle and knee joint centers were calculated as midpoints between the malleoli and femoral epicondyles, respectively. The hip joint center was calculated using the regression model from Bell et al (11), based on anterior and posterior superior iliac spine markers. Participants walked at self-selected speeds, which were similar across conditions. Using an inverse dynamic approach Visual 3D (C-Motion), we calculated the first peak KAM normalized to a participant's mass (Nm/kg) and averaged across the 5 trials. In addition, subjects were asked about the comfort of each condition and whether they noted any immediate effect on knee pain.

A subject was characterized as a biomechanical responder if, for the study knee, there was a ≥2% reduction of their KAM with the lateral wedge insole compared to both that with their own shoe and that with the neutral insole. Biomechanical responders were eligible for the study. We chose a 2% reduction as it was above the minimal detectable difference in KAM (12) and was a reasonable approach to ensure biomechanical response.

Eligible subjects were randomized by a statistician who had no contact with study staff and created sealed opaque envelopes for each study ID number, to be opened when a subject entered the study. The randomized allocation list used to create the envelopes was a single-allocation computer-generated list of balanced permuted blocks with a block size of 6. Study staff were blinded with regard to block size. Subjects were randomized 1:1 to 1 of 2 treatment sequences (AB or BA) in a 2-period crossover trial. Each randomized participant was provided either a 5° lateral wedge insole (A) or a neutral insole (B), for 8 weeks, followed by an 8-week washout. Next, they switched to the other treatment for 8 weeks. The initial insole treatment was removed at the last visit of the assigned treatment period in order to prevent treatment contamination. Both insoles had a density of 70 Shore A.

Participants attended the clinic for 5 visits: a screening visit (2 weeks prior to baseline), baseline visit (0 weeks), posttreatment visit (8 weeks), post-washout visit/second baseline visit (16 weeks), and second posttreatment visit (24 weeks). Participants were asked to wear insoles at least 4 hours per day but could wear them for as long as they wanted.

Bone marrow lesions (BMLs) appear on knee MRI in regions where excessive loading has produced bone damage. Medial lesions predominated in those with medial OA. BMLs in the PF joint shrank over 6 weeks when focal loading was reduced in that area (13), suggesting that BMLs may respond to unloading treatments. We evaluated subjects for change in BML volume in the medial joint. At baseline, patients underwent MRI of the study knee; this was repeated at 8 weeks, 16 weeks, and 24 weeks. Using a Philips Achieva 3.0T scanner, we obtained sagittal images using spectral attenuated inversion recovery fat suppression, with repetition time 4,300 ms, echo time 50 ms, field of view 16 × 24 cm, matrix 212 × 220 pixels, slice thickness 3 mm with 0.3-mm gap, and bandwidth 621–655 Hz/pixel.

Outcome measures: pain. The primary prespecified symptom outcome measure was overall pain in the knee in the

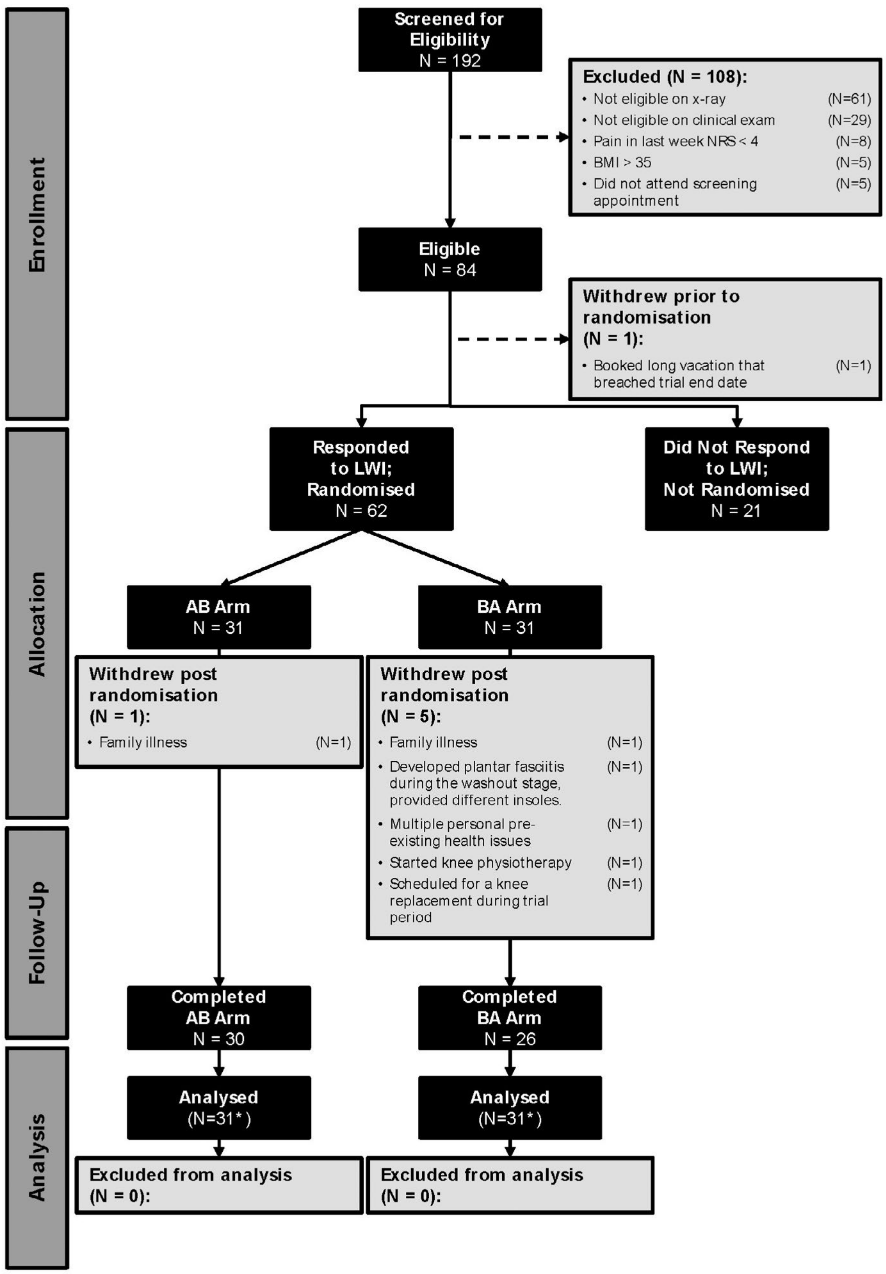

Figure 1. Disposition of the patients in the lateral wedge insole (LWI) trial. * = multiple imputation was used to estimate missing values for patients, accounting for a greater number of patients than completed the trial. NRS = numerical rating scale; BMI = body mass index.

past week, scored using a numerical rating scale (0–10) as per recommendations of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) group (14). At baseline, subjects were also asked to identify the activity that provoked the most knee pain and to score pain during this activity at each visit (15). Finally, we administered the Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire at each visit (16).

Outcome measures: structure. Technicians at Imorphics, who were blinded with regard to treatment assignment, manually segmented BML volumes in paired images from each patient's knee. BMLs were outlined on each MRI slice and the volume integrated over all slices. For sagittal images, on which we based results, technicians segmented BMLs in the patella, femur, and tibia. The intraclass correlation coefficient for interobserver reliability for BML volume was 0.91 ($P < 0.001$) (13). The primary structural outcome measure was change in medial BMLs. We defined these as BMLs involving either the tibia medial to the cruciate ligaments or the femur medial to the notch, using regions derived from the Whole-Organ Magnetic Resonance Imaging Score (17).

Sample size. We aimed to detect a treatment effect size (Δ) of 0.4 SD with 80% power (2-sided alpha level 0.05). Based on a within-patient SD of 2.4 for overall pain in the past week (18) while testing a lateral wedge insole, this effect size represents a difference of 1 point on this knee pain rating scale and translates to a sample size of 52 subjects completing the trial. We assumed 10% loss to follow-up and aimed to randomize 58 subjects.

Statistical analysis. Our analysis followed an intent-to-treat approach. Multiple imputation by chained equations was used to correct estimates for bias due to missing data, assuming data were missing at random. To assess the difference in treatment effects between the two insoles, we used maximum-likelihood mixed-effects multiple linear regression models. The primary analysis model used overall pain in the last week (measured at the end of each treatment visit) as the outcome measure, which was adjusted for baseline (pretreatment visit) pain scores. Using the baseline value as a covariate (the analysis of covariance approach) is a recommended methodology with less bias and greater power to detect differences (19). Participant identification was included as a random effect. To test for carryover effects, we included 3 additional covariates: a treatment term, a period term, and a treatment-by-period interaction term (the term testing for carryover). We ran a second analysis model identical to the first except that the period and treatment-by-period interaction terms were removed.

The same regression models were used to analyze the secondary outcome measures, using the same terms but replacing "overall knee pain during the past week" with the specific secondary outcome measures. In addition to evaluating the response to insoles on a continuous scale, we defined responders as those who achieved an accepted minimally important difference in overall knee pain of 1 on the 0–10 scale (20). We examined the percentage of trial participants who achieved responder status according to this definition, using the change in the pain score at the beginning of the period to the pain score at the end of the period.

Table 1. Differences in KAM using patient's own shoes, neutral insoles, and lateral wedge insoles, among biomechanical responders and biomechanical nonresponders*

	Own shoe, mean ± SD	Neutral insole, mean ± SD	Lateral wedge insole, mean ± SD	Difference between own shoe and lateral wedge insert, adjusted mean (95% CI)	Difference between neutral insole and lateral wedge insole, adjusted mean (95% CI)
Nonresponders (n = 21)					
KAM difference, absolute value	0.54 ± 0.17	0.54 ± 0.16	0.55 ± 0.17	0.01 (0.00, 0.02)	0.00 (−0.01, 0.02)
KAM difference, %	–	–	–	1.98 (−0.07, 4.03)	0.64 (−2.12, 3.39)
Immediate pain†	2.86 ± 2.46	2.33 ± 2.35	2.05 ± 2.09	−0.78 (−1.28, −0.28)	−0.27 (−0.77, 0.23)
Immediate comfort†	7.29 ± 1.74	7.10 ± 2.21	7.62 ± 1.77	0.35 (−0.18, 0.88)	0.22 (−0.32, 0.75)
Responders (n = 62)					
KAM difference, absolute value	0.50 ± 0.15	0.49 ± 0.15	0.46 ± 0.14	−0.04 (−0.04, −0.03)	−0.03 (−0.04, −0.03)
KAM difference, %	–	–	–	−7.54 (−8.53, −6.55)	−6.56 (−7.69, −5.42)
Immediate pain†	3.03 ± 2.21	2.84 ± 2.06	2.48 ± 1.89	−0.28 (−0.57, 0.02)	−0.18 (−0.48, 0.11)
Immediate comfort†	7.00 ± 1.87	7.32 ± 1.94	7.44 ± 1.77	0.14 (−0.21, 0.49)	0.12 (−0.22, 0.47)

* KAM = knee adduction moment; 95% CI = 95% confidence interval.
† Immediate pain and comfort graded on a 0–10 scale. For pain, lower scores represent less pain, and for comfort, higher scores represent more comfort.

RESULTS

Of the 83 participants who satisfied inclusion criteria and were evaluated in the gait laboratory (Figure 1), 62 were biomechanical responders. In this group, the mean reduction in KAM with lateral wedge insoles compared to neutral insoles was 6.6% and compared to their own shoes was 7.5% (Table 1). In contrast, 21 participants (25.3%) were biomechanical nonresponders, and their mean KAM was 2% higher with the lateral wedge insoles than with their own shoes (Table 1). There were no differences between responders and nonresponders in immediate knee pain upon walking in the laboratory or in the comfort of their own shoes versus the lateral wedge inserts. Randomized participants were on average 64 years old, had a mean BMI of 28 kg/m^2, and the majority were men (Table 2). Of the 62 randomized participants, 59 completed the first treatment period and 56 completed the second treatment period.

We found no significant evidence of carryover effects for any of the outcome measures of interest. When we examined our primary outcome measure, we found that patients reported less knee pain when randomized to receive lateral wedge insoles than when using neutral insoles (mean difference in pain score 0.7 [95% CI 0.1, 1.2]; P = 0.02) (Figure 2 and Table 3). The pain during participants' most painful nominated activity was also less severe during the period that they used lateral wedge insoles (Table 3). However, we did not find significant differences between neutral insole use and lateral wedge insole use in KOOS pain scores or other KOOS subscales. We found no effect of treatment on medial BML volume or on total BML volume in the knee (Table 3). Results from complete case analyses were similar.

Table 2. Characteristics of biomechanical responders and nonresponders*

	Responders (n = 62)	Nonresponders (n = 21)
Age, years	64.18 ± 9.10	65.86 ± 10.03
BMI, kg/m^2	28.21 ± 3.44	28.56 ± 3.99
Women, no. (%)	23 (37.10)	9 (42.86)
HADS anxiety score†	12.17 ± 2.24	12.48 ± 1.57
HADS depression score†	9.10 ± 1.24	8.33 ± 0.97
Overall knee pain during past week (0–10 range)	5.26 ± 1.63	5.24 ± 1.87
Pain during nominated activity (0–10 range)	6.18 ± 1.54	6.05 ± 1.66
KOOS pain subscale score (0–100 range)‡	55.20 ± 13.45	58.07 ± 12.07
K/L grade of studied knee, no. (%)		
Grade 2	17 (27.4)	–
Grade 3	37 (59.7)	–
Grade 4	8 (12.9)	–

* Except where indicated otherwise, values are the mean ± SD. BMI = body mass index; K/L = Kellgren/Lawrence.
† Hospital Anxiety and Depression Scale (HADS) scores ranged from 0 to 21, with higher scores (>11) indicating either anxiety or depression.
‡ Knee Injury and Osteoarthritis Outcomes Scores (KOOS) ranged from 0 to 100, where 100 represents no pain/difficulty.

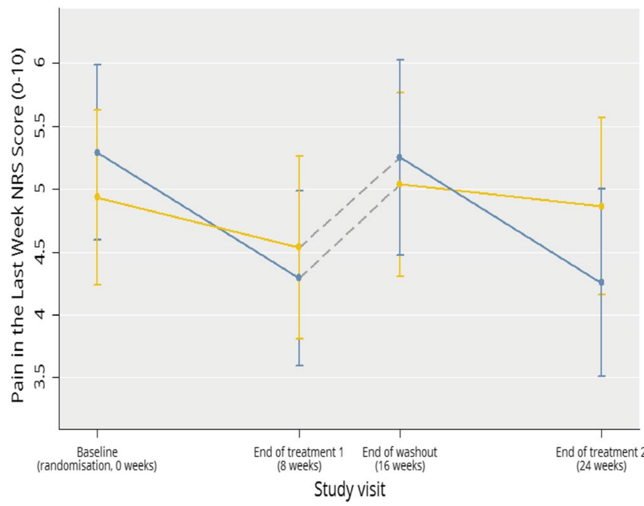

Figure 2. Crossover change in overall knee pain during the past week, assessed based on a numerical rating scale (NRS) of 0–10. Blue lines indicate lateral wedge insole, yellow lines indicate neutral insole, and broken lines indicate the washout period. Values are the mean and 95% confidence interval.

During the period of active treatment with lateral wedge insoles, 28% of participants (16 of 57) achieved a minimally important improvement, and with neutral insoles, 22% (13 of 58) experienced this level of improvement. The odds ratio for achieving important improvement while using lateral wedges versus neutral inserts was 1.35 (95% CI 0.58, 3.13) (P = 0.49). Participants reported a mean ± SD insole usage time of 7.10 ± 2.72 hours/day at the end of the first treatment period and 7.80 ± 3.17 hours/day at the end of the second treatment period.

During the trial, 7 participants experienced side effects leading to temporary (3 participants) or permanent (4 participants) treatment discontinuation. Of these instances, 4 occurred during lateral wedge insole treatment and 3 during neutral insole treatment. Of the 2 participants who discontinued treatment with lateral wedge insoles, 1 had calf pain at night and the other experienced worse knee pain. Of the 2 participants who stopped using neutral insoles, 1 developed a toe blister and the other had worsening knee pain.

DISCUSSION

In this trial, we prescreened subjects for select biomechanical responses to lateral wedge insoles. When we excluded those who either had PF involvement or failed to show biomechanical

Table 3. Comparison between lateral wedge insole and neutral insole after 8-week treatment*

Outcome	Posttreatment adjusted mean (95% CI) Lateral wedge insole	Neutral insole	Difference between treatments, mean (95% CI)
Pain during past week†	4.16 (3.69, 4.62)	4.85 (4.42, 5.28)	0.70 (0.12, 1.27)‡
Pain during nominated activity†	4.80 (4.30, 5.31)	5.77 (5.28, 6.26)	0.97 (0.32, 1.61)§
KOOS score¶			
Pain subscale	60.66 (57.21, 64.11)	58.82 (55.67, 61.96)	−1.84 (−6.31, 2.62)
Symptoms subscale	60.64 (57.59, 63.70)	59.41 (56.40, 62.42)	−1.23 (−5.11, 2.65)
Activities of daily living subscale	66.29 (63.15, 69.44)	65.01 (61.88, 68.14)	−1.28 (−5.19, 2.62)
Sports and recreation subscale	43.57 (39.46, 47.67)	42.21 (37.56, 46.86)	−1.36 (−6.97, 4.26)
Quality of life subscale	44.18 (40.62, 47.73)	44.09 (40.80, 47.38)	−0.09 (−4.64, 4.47)
Total BML volume	12,959.66 (10,991.04, 14,928.29)	11,047.29 (8,833.52, 13,261.05)	−1,912.38 (−4,602.61, 777.86)
Medial BML volume	8,331.48 (6,903.42, 9,759.55)	7,051.42 (5,398.37, 8,704.47)	−1,280.07 (−3,210.91, 650.78)
Lateral BML volume	1,340.93 (801.87, 1,879.99)	1,219.47 (648.63, 1,790.32)	−121.45 (−630.27, 387.36)

* Pain ratings and other scores were adjusted for the baseline value of the relevant outcome measure, which was the same for both treatment groups. 95% CI = 95% confidence interval; KOOS = Knee Injury and Osteoarthritis Outcomes Scores; BML = bone marrow lesion.
† Lower scores represent pain reduction.
‡ $P = 0.02$
§ $P = 0.003$
¶ Higher scores represent pain reduction.

responses to lateral wedge insoles, we detected a small effect of these insoles on pain reduction that was missed in previous trials in which there was no prescreening. However, most participants in the trial did not experience a level of improvement that would qualify as minimally important based on accepted thresholds. While this trial suggests an approach to detect efficacy of this treatment, the efficacy was not sufficient to recommend this treatment or the screening approach we used. In this case, we may have found a treatment that shows statistical significance without clinical significance.

The small treatment effect we found may account for the lack of consistency across outcome measures. While the lateral wedge insole reduced knee pain based on our primary outcome measure (knee pain during the past week) and also led to pain reduction in the patient's nominated most painful activity, it did not significantly reduce pain or self-reported function that was assessed using the KOOS survey, an expanded version of the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) (21). We have reported that the WOMAC is not as sensitive to change as are global questions about knee pain (15), which may partially explain the lack of effect. However, this lack of effect also suggests that the treatment effect was modest. For the primary outcome measure, the effect size calculated as a standardized response mean was 0.30. This effect is comparable to that found for nonsteroidal antiinflammatory drugs versus acetaminophen in OA pain treatment (22). While a validated estimate of minimally important improvement (20) for our primary outcome measure was 1.0, the mean difference in pain reduction between the lateral wedge and neutral insole periods of treatment was only 0.7.

Our screening process utilized a gait laboratory to identify participants who had a biomechanical response to wedge insoles. Such laboratory evaluations are expensive and may not be widely available. Clinical screening protocols could be developed that might identify, with high probability, those likely to respond. We have tried to develop such a protocol without success (23), and other efforts are needed. While the KAM measures the medial versus lateral load, another factor affecting medial joint loading is the knee flexion moment. We have previously reported that the lateral wedge insole used in this study does not affect this moment (24).

Once PF OA is ruled out by a simple physical examination, given the low cost and benign safety profile of these wedges, it might be argued that treating patients with these insoles is a reasonable clinical strategy, rather than seeking a gait laboratory evaluation. Even so, the treatment effect is likely to be small, and only a few patients may experience substantial benefit. Could the effect of lateral wedge insoles have been similar to those seen in previous trials that used the WOMAC or KOOS as outcome measures? In two large studies using variable stiffness shoes or lateral wedge insoles (5,18), authors used the same global knee pain measure and found no effect of treatment (versus control) on pain.

Osteoarthritis is challenging to treat because it combines mechanopathology with an inflammatory response to joint injury, both of which contribute to pain and disease progression. It has been unclear whether nonsurgical treatments targeting pathomechanics were likely to be major elements of the treatment regimen. Knee brace adherence is poor, for example. Our findings offer modest promise for a simple, inexpensive treatment. Further refinement of the treatment with use of specific shoes or increases in the degree of wedging may increase efficacy.

We and others have reported that biomechanical response to lateral wedge insoles is variable (24–26). Although the reasons are unclear, one study suggests that stiffness in feet and ankles in some individuals may prevent the lateral ankle eversion that is necessary for knee loading to change with this treatment (25). While lateral wedge insoles are thought to be safe treatments, their use occasionally generates reports of discomfort in the foot (22) and may cause back pain (20). In the present study, we did not find major safety concerns, and no one discontinued treatment due to back pain.

In this crossover trial, we sought to evaluate the effect of lateral wedge insoles. Crossover trials permit the testing of treatments more efficiently than parallel design trials and make it easier to detect modest effects of treatments.

In summary, we found, for the first time, that lateral wedge insoles may be modestly effective in reducing pain in patients with medial knee OA. However, the treatment effect was small and most treated patients did not achieve conventional levels of minimally important response. Future modifications of the screening strategy or treatment might offer greater levels of efficacy.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Felson had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Felson, Jones.
Acquisition of data. Carter, Liu, Callaghan, Hodgson, Bowes.
Analysis and interpretation of data. Parkes.

ADDITIONAL DISCLOSURES

Author Bowes is an employee of Imorphics, Ltd.

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